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Original Research

Health risk assessment of indoor volatile organic compounds considering long-term trend of volatile organic compound

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ABSTRACT

Background: The indoor air quality is among other things determined by air pollutants such as volatile organic compounds (VOCs) which are associated with health effects. The severity of these health effects depends on the kind and part of the specific chemicals within the VOC group. Since the 90th the expected health risk has been evaluated using the VOC sum concentration under the assumption of a fixed composition with a clear defined part of every single VOC. The question is whether the VOC sum and whether the share of individual VOCs have been changed over the recent years. **Methods:** Indoor VOCs were measured within the frame of epidemiological studies from 1994 until 2008. In addition, a large number of apartments were investigated depend on inquiries by physicians, health offices, or inhabitants in a period from 2009 to 2014. The human health risk was assessed both based on currently valid criteria and based on adapted criteria considering the potential composition of the VOC pattern. **Results:** A substantial reduction in the sum of VOCs (about 60%) could be demonstrated caused by a clear decreasing trend of aromatics and alkanes. No such changes could be observed for cycloalkanes, chlorinated hydrocarbons, and terpenes. The resulting pattern of VOC is quite different compared with the start situation in 1994. The part of terpenes at the VOC sum increased by two from approximately 25% (1994) to 55% (2014). Due to the decrease of the VOC sum, the human health risk might be underestimated if the VOC sum is the only criterion. **Conclusions:** Based on our findings special attention should be paid to groups of VOCs and/or single VOCs.

KEY WORDS: Environmental medicine, gas chromatography/mass spectrometry, human health risk assessment, indoor air quality, indoor volatile organic compound, long-term trend passive sampling

INTRODUCTION

Signs and symptoms of ill health may be associated with indoor volatile organic compounds (VOCs) [1-8]. Although the associations of VOCs to ill health have been controversially discussed [9,10], some data show that even small dosages may already account for these observed adverse health effects [2,4,8]. For this reason, VOCs are important in the regulation of indoor air quality.

How to assess health relevance of measured VOCs? In a first step, the relevance can be judged using the sum concentration based on the assumption that specific VOC groups contribute to the VOC sum concentration in a fixed part. The fixed part considers the different "toxicological" properties of the contributing VOCs. If the share of single VOCs has been changed over the time, it is impossible to judge the VOC sum concentration using the up to now underlying threshold value. Therefore, it is necessary to know whether the parts of VOCs have changed in any way (concentration and/or proportion of its components).

In this context, long-term trend studies are useful in the assessment and the trend control of the indoor VOCs burden [11]. Furthermore, this kind of study is suitable for disclosure of changing of the time trend of a single VOC which contribute predominantly to the VOC sum. This fact is of importance especially for those components which are routinely quantified for local health departments. To reveal contributions of indoor VOCs to health disorders, investigations were directed to assess indoor air exposure using measurements of a standard mixture of VOCs. This standard mixture is based on a mixture proposed by Molhave *et al.* [12] to control the indoor air environment.

Considering these facts, the aim of this study was to find out whether the trend of the absolute concentration of different VOC groups and of the relative ratios between VOC groups have undergone changes over a past 15-year period. Furthermore, it should be shown whether the use of up to now underlying threshold values leads to a misinterpretation of the existing situation.

It should be pointed out explicitly that the presented paper only deals with the description of the VOCs exposure, the rule of threshold values, but not with resulting health effects.

METHODS

VOCs were measured as part of several epidemiologic studies [13-16] in the participants' residences. The studies were approved by the ethics committee of the University of Leipzig.

4725 participants were involved in the study, and 2679 individual measurements were performed during 15 years (1994 until 2008). Starting in 2009, 41 additional apartments have been investigated. The exposure situation close to human was assessed for a variety of reasons, primarily because of clarification of their potential health effects. These measurements are part of a long-term case–control study. This study tries to objectivize the causes suspected by the patients, mainly indoor air exposures.

Sampling

All measurements were taken using passive samplers [17]. The advantage is to record a mean load over a sampling period of a longer time, usually 4 weeks. Therefore, this method avoids short time peaks. The passive samplers were deposited in those rooms of residences in which the families according to their own statements spent the most of their time; this mainly concerned the living room or bedroom. The information regarding the room was gathered by an epidemiological questionnaire.

In case of the measurements within the frame of the epidemiological studies, it was ensured according to the design of the epidemiological studies that all types of houses or apartments and all measurement times are similarly distributed. That means, in particular, that no week, day or season is overrepresented. Table 1 shows the distribution per year of the carried-out measurements.

Analysis

The method is described in detail [16,18,19]. Briefly, after extraction of the VOC-coated active charcoal layer of the 3 M passive sampler a quantitative VOC analysis using gas chromatography (GC) was performed (Autosystem-GC, Perkin Elmer, Flame ionization detector/electron capture detector, mass spectrometry detector).

In the following assessment and for reason of comparability only those 26 components for which a complete set of data was available are included [Table 2]. These 26 VOCs are alkanes (heptane, octane, nonane, decane, undecane, dodecane, tridecane), cycloalkanes (methylcyclopentane, cyclohexane, methylcyclohexane), aromatics (benzene, toluene, ethylbenzene, m-, p- and o-xylene, styrene, 2-, 3-, 4-ethyltoluene), chlorinated hydrocarbons (chlorobenzene, trichloroethylene, tetrachloroethylene), and terpenes (α- and β-pinene, limonene, carene).

Statistical Analyses

The statistical analyses were performed using Statistica [20] and Excel [21].

The trend was calculated using the Mann-Kendall-test. This test is a nonparametric test and examines the signs of pairwise differences of the VOC time series.

RESULTS

The sum concentration of all VOCs (VOC sum) is determined by the 3 subgroups alkanes, aromatics, and terpenes. The part of them at the VOC sum concentration is higher than 85% (mean±SD: 91±3%) depending on the year of investigation. Therefore, the presentation of the results will be focused on these 3 subgroups.

Concentration Trends (Absolute)

VOC sum is shown in Figure 1. The last dot represents the mean between 2009 and 2014 (case-control study).

Table 1: Annual distribution of measurements

Year	1994	1995	1997	1998	1999	2000	2001	2004	2007	2008	2009-2014
n	88	266	158	286	287	100	556	377	312	249	41

Table 2: Target values for VOC groups under investigation

VOC group	Alkanes	cyclo-alkanes	Aromatics	ClHC	Terpenes	VOC sum
Target value [$\mu g/m^3$]	40	15	66	3	30	154

VOC: Volatile organic compounds

The trend test (Mann-Kendall trend test) was applied on the results of measurements obtaining from epidemiological studies only. The test showed a significant decrease for all VOC sums ($P = 0.05$) and for aromatics ($P = 0.02$), as well as a demonstrable reduction for alkanes ($P = 0.08$ trend).

The group of cycloalkanes, chlorinated hydrocarbons, and terpenes do not indicate any time-dependent trend change [Figure 2].

Regarding the individual VOC components, the most significant trend was seen for toluene ($P = 0.02$), o-xylene ($P = 0.03$) and 3-ethyltoluene ($P = 0.03$).

Trends of the Concentrations of the Proportional Compounds (Relative)

Independent from the general decrease of the VOC sum exposure, the proportion of individual substances to the total burden shows a clear shift. The proportions of the different VOC subgroups are shown in Figure 2. On one hand, the proportions of alkanes and aromatics decrease, and on the other hand, the proportion of terpenes showed an increasing trend [Figure 2].

Figure 3 demonstrates these findings divided into 3 time periods: Before 1997, between 1997 and 2008, and 2008 until

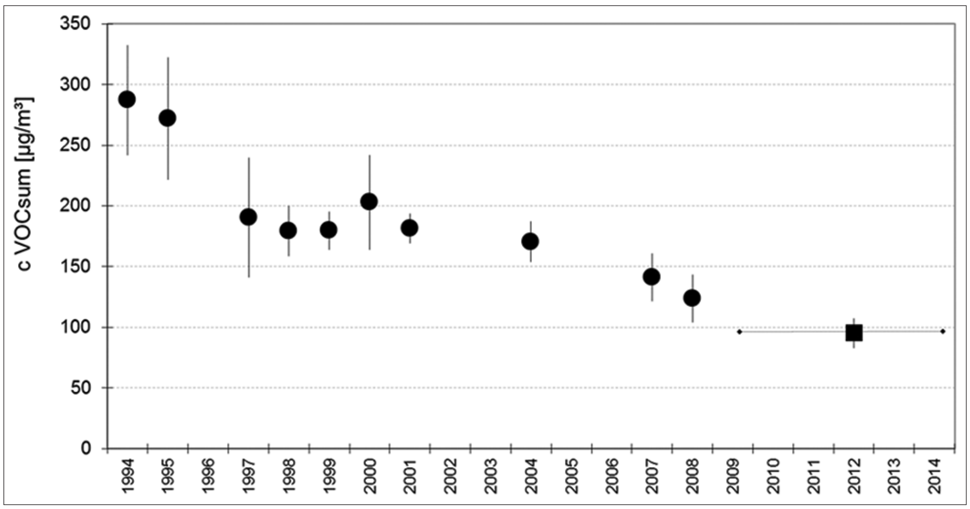

Figure 1: Temporal course of the volatile organic compounds sum concentration 1994-2014 (±95% CI standard error of mean) standard error of mean

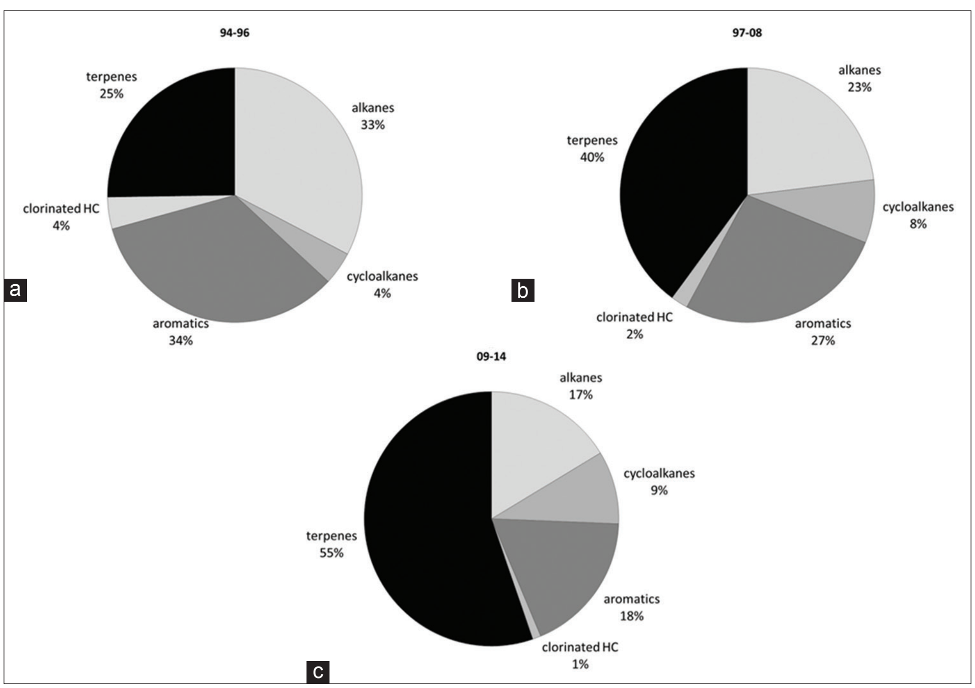

Figure 2: (a-c) Time trend of the shares of different subgroups of volatile organic compounds between 1994 and 2014

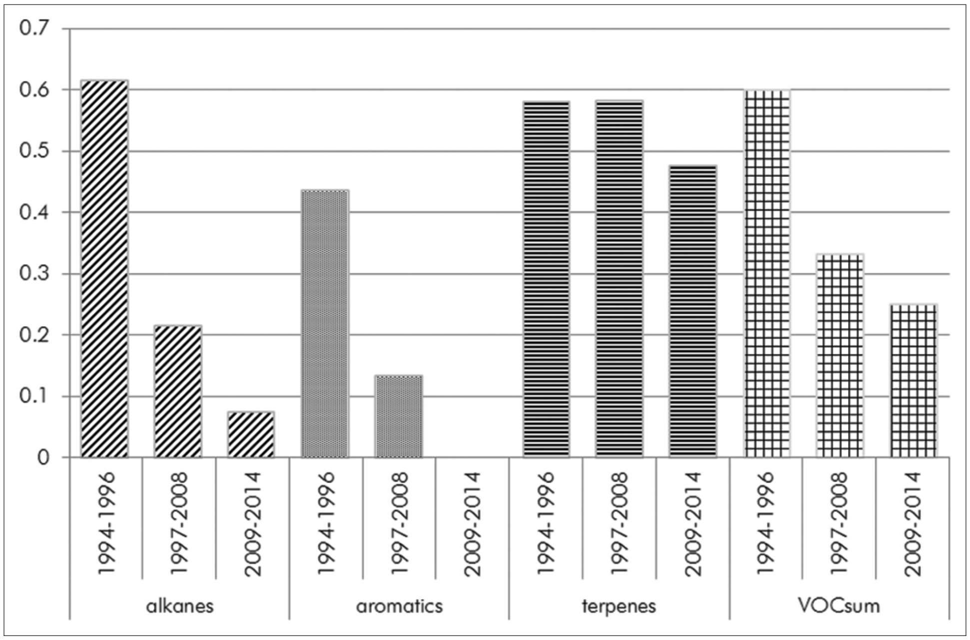

Figure 3: Excess frequencies (total) dependent on time and kind of volatile organic compounds

2014. This classification considers two key points: In 1996, a new regulation was brought into force which regulates and reduces the use of aromatics. The study design before and after 2008 was different because of two different fundamental questions as explained before.

Health Risk Assessment

The second question pertains to the problem of human health risk assessment. What happens if the up to now valid threshold values will be used to assess the health risk coming from VOC exposure without the knowledge of the time trend and without the knowledge of the shown contribution of different VOC/VOC subgroups to the VOC sum.

Different assessment criterions are possible. Assessment schemes base on both VOC sum (or total VOC concentration) and single VOCs. The following details [22] in which target values are mentioned for each VOC which we have measured. These values are consensus values and valid until now. These values are an evaluation tool to assess the indoor air quality considering human health.

Regarding the measured VOCs the target values are shown in Table 2.

Based on the target values shown in Table 2, the following picture emerges [Table 3].

The excess frequency of VOC sum decreases from 60% (1994-1996) to 33% (1997-2008) to 25% (2009-2014).

The question is whether the excess frequency of VOC sum also describes the excess frequency of the subgroups or whether the finding is valid for all or selected subgroups.

Table 3: Time dependent excess frequency [%] for VOC subgroups in case no exceeding of VOC sum

Subgroups	1994-1996	1997-2008	2009-2014
Alkanes	19	6	3
Aromatics	3	1	0
Terpenes	22	42	33

VOC: Volatile organic compounds

DISCUSSION

Figures 1-3 have to be interpreting in context. Whereas a decreasing grant, in general, was observed [Figures 1 and 3], the proportion of terpenes is substantial increase [Figure 2]. In addition, the decrease is much lower in case of terpenes compared with the other subgroups - alkanes and aromatics. From that point of view, a special focus should be laid on terpenes also for further regulations.

In this work, we observed a clear long-term trend for the concentrations of the VOC sum and for distinct VOC subgroups. With our recorded changes in the constitution of the overall VOC exposure, it can be assumed that this could cause in different health effects.

The current findings show a noticeable decrease in the total VOC sum of the determined dwellings. This decline concerns, in particular, the subgroups alkanes and aromatics. In the period between 2009 and 2014, the sum concentration was only 35% of the concentration in 1994.

One major reason for these changes was already addressed in the context of the division in the three time periods. Beginning in the mid-1990s, solvents with a low boiling point generally used in the commercial/industrial production of lacquers and paints were replaced by glycols and higher alkanes. Hence, these compounds do not fall under the common definition of solvents (boiling point <200°C) and can be possibly delivered about several months or years in the interior air; meanwhile there is a reduction of the "classical" solvents.

- Toluene and higher alkanes represent the main part of the VOC sum. For example, We identified a massive decline for toluene from 83 μg/m^3 in 1995/96 to 23 μg/m^3 in the following year 1997. This fact based on the new guidelines for toluene which was introduced in Germany in 1996 [23]. Afterward, the drop from 23 μg/m^3 to 15 μg/m^3 in the time period from 1999 to 2008 was much less dramatic. Other emission classes that could occur in the indoor air, e.g., long chain alkanes, branched alkanes, or glycols was not examined. However, the analyzed chromatograms revealed peaks of higher C_{14}-C_{16} alkanes with elevated levels. This remains a speculation until broad epidemiological studies have been carried out.
- Additional aspect is, that may be the additives of the solvents for indoor paints and lacquers, including glues (e.g., floor coverings) have undergone changes in their composition.
- Furthermore, the work in the prevention could have brought success. We started information campaigns for young parents about the regular use of solvents or solvent containing materials and using with strongly VOC-burdened products. In 1996, the first consent discussions with the parents took place as a result of our first epidemiologic study [13].

Another rising problem is the increase of VOC resulting from microorganisms, like mold, in the indoor air. This topic based on the more and more interlocking of the interior and furthermore of the reduced air exchange rates. Molds produce specific secondary metabolites during their growth which are described as microbial VOCs (MVOCs). These compounds include a wide range of chemical classes such as alcohols, alkenes, ketones, ethers, esters, mono- and sesquiterpenes [24]. Up to now, it could be detected about 200 compounds emitted by mold [25,26]. In contrast to the "classic" VOCs, the MVOCs occur only in very low concentrations in the indoor air, approximately up to 1 μg/m^3. The main indicator MVOCs for a microbial contamination in the indoor are 3-metyhlfuran, dimethyl disulfide, 1-octen-3-ol, 3-octanone, and 3-methyl-1-butanol [27]. However, there still exist additional MVOCs which are less specifically for ensured mold evidence because they can also be attributed to building materials, paint, human activities, and combustions processes such as smoking and fire [28].

A big problem is the human health risk assessment based only on the VOC sum. If the health risk is assessed only using the VOC sum, the overall VOC exposure would be underestimated in a lot of apartments. If this assessment is based on particular subgroups, e.g. elevated concentrations of terpenes, health risks might be realized. In total, the VOC sum criterion was exceeded in nearly 60% in the 1990s and in 25% after 2009. If the VOC sum criterion was met concurrently, the excess over the terpenes criterion was increased from 22 to 33%.

Terpenes are known to have sensitizing properties. From that, we may derive that the profile regarding health risk has been changed from an irritating to a sensitizing profile. To assess the human health risk, it seems to be more and more necessary to come from a more integrative risk assessment (based on the VOC sum criterion) to an individual judgment of VOC subgroups and/or single substances.

Study Limitations

- The complete time series could only be generated for the considered 26 VOCs [15,17]. It cannot be excluded that other than the measured VOCs show a different trend.
- The different sample size per year during the study period may lead to different levels of significance but can be neglected since the sample size in all cases was higher than 100 except 1994 [Table 1] and the time span between 2009 and 2014.

Main Advantages

- The study includes a very large number of measurements over a time period of 15 years. No time of year and/or type of apartment/house is over represented due to the applied study design.
- The passive sampling over 4 weeks ensures that activities and peak concentrations generated by short time emissions (e.g., of smoking, lifestyle events, etc.) did not influence the results in a significant way (short-term influence versus long-term average).

It should be addressed in further studies to what extent the results can be transferred to other regions.

CONCLUSION

Since the composition of VOC subgroups has been changed a health risk assessment based on the same total using the VOC sum concentration compared with that 20 years ago, leads to an incorrect judgment. Therefore, the VOC limit concentration depends on the specific composition of the VOCs. Since at the present days dominating proportion of terpenes on the VOC sum and showing health effects also at lower concentration, the situation concerning VOC has been changed totally coming from a combined irritative-sensitizing to a dominant sensitizing profile.

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